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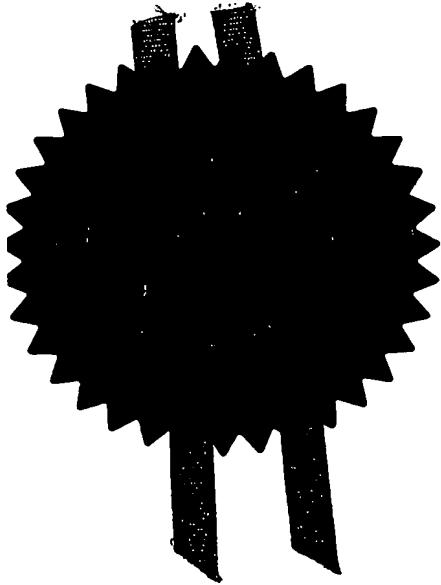
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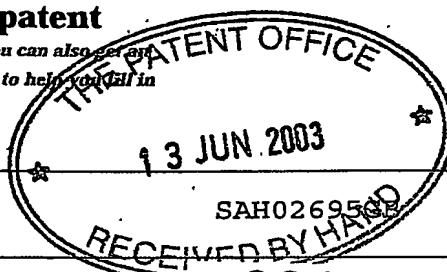
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1. Your reference


 16 JUN 03 E815001-5 D02890  
 P01/7700 0.00-0313759.3

 2. Patent application number  
*(The Patent Office will fill in this part)*

0313759.3

13 JUN 2003

 3. Full name, address and postcode of the or of  
 each applicant (*underline all surnames*)

 The Technology Partnership plc  
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6746044001

Patents ADP number (*if you know it*)
 If the applicant is a corporate body, give the  
 country/state of its incorporation

United Kingdom

4. Title of the invention

Fluid Sampling Components

5. Name of your agent (*if you have one*)

Gill Jennings &amp; Every

 "Address for service" in the United Kingdom  
 to which all correspondence should be sent  
*(including the postcode)*

 Broadgate House  
 7 Eldon Street  
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Patents ADP number (*if you know it*)

745002

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Country

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 Date of filing  
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 7. If this application is divided or otherwise  
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 8. Is a statement of inventorship and of right  
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NO

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Description 11

Claim(s)

Abstract

Drawing(s)

7 + 7 *fh*

10. If you are also filing any of the following, state how many against each item.

Priority documents

Translations of priority documents

Statement of inventorship and right to grant of a patent (Patents Form 7/77)

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Request for substantive examination (Patents Form 10/77)

NO */*

Any other documents (please specify)

11. For the applicant

Gill Jennings & Every

I/We request the grant of a patent on the basis of this application.

Signature *Michael Brunner*

Date

13 June 2003

12. Name and daytime telephone number of person to contact in the United Kingdom

BRUNNER, Michael John  
020 7377 1377

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## Fluid Sampling Components

This invention relates to components for use in an apparatus for detecting and analysing biological agents in animal body fluids, for instance milk. More specifically, 5 the present invention relates to a fluid-sampling device, fluid sample transportation means (temporary fluid storage means) and a fluid sample collecting device.

In recent times it has been realised that there is a benefit in monitoring collected animal body fluids, such as milk from dairy cattle, for the presence of certain chemicals or hormones. For example, it can be beneficial to monitor the milk of a cow to detect 10 the presence and level of progesterone in order to determine its ovulating cycle. Alternatively, there may be a need to monitor the milk to detect for other types of bio-markers, such as chemical imbalances that are indicative of a disease in the cow or other animal.

Monitoring collected animal body fluids for the presence and concentration of 15 hormones, and in particular progesterone, is known. By frequent analysis of progesterone levels in milk samples from a particular animal, ovulation cycles can be mapped. Similarly monitoring of luteinising hormone levels in milk samples gives another method for mapping an animal's ovulation cycle.

Examples of other types of bio-markers that are known to benefit from 20 monitoring, include: NAGase activity, which can indicate that an animal is stressed or suffering from sub-clinical mastitis; ketone levels, which indicates whether an animal may have ketosis; corticosteroids, which indicate stress levels; and antibiotics or other medical compounds. Bio-markers can also indicate response to the presence of a disease, for example bovine viral diarrhoea virus (BVDV) or Leptosporosis (Weil's 25 disease), and can be used to detect ovarian dysfunction. Detection of disease vectors can lead to early treatment of the disease and the prevention of spread of infectious diseases to other animals. As a further example, milk and cells contained within it may be analysed for genetic properties.

Sampling of farm animals and measurement of these bio-markers by specialists 30 (in particular veterinarians) on the farm, within veterinary practices and within analytical laboratories is typically expensive and time-consuming.

Specialist knowledge and expertise is needed: to identify from which animals to sample and measure the bio-marker; to take a sample of body fluid; to undertake the assay to measure the bio-marker; and to process the results of the assay and suggest 35 appropriate action.

The farm environment presents additional problems. Testing on farm premises has been seen as unfeasible due to the difficulty of achieving satisfactory precision and

because of the time the farmer can afford to spend performing the tests manually.

Prior art testing apparatus is large, awkward and expensive or limited to robotic milking or appropriate only for scientific research.

There has been a considerable amount of research and development in terms of automating animal milk collection. Systems which gather milk automatically and then monitor for the presence of bio-markers (biological or chemical agents) in an automatic manner have been produced, however these systems have various disadvantages which affect the efficiency of the sampling and the extent to which analysis can be performed.

10 In known milking systems, samples are taken, for example, by opening a valve in the milk line of each cow for a predetermined time. This sample milk can then drop (via gravity) onto analysing means or can be passed along tubes to a separate component which stores the milk samples for later analysis off line. Commercially available systems require human intervention to identify, transfer and label sample pots.

15 In prior art sample analysis systems the assays of interest have been predetermined by the design of the system and have a fixed sampling regime which cannot be adapted at will. There is no provision of a sample ordering system which keeps track of specific samples so that they may only be directed for analysis of selected assays. In prior art systems, the samples are analysed generically and there is no way of specifying or altering the path of the samples. If one or some of the animals are suspected of having a certain disease or deficiency, there is no way of analysing the samples of these animals immediately and then deciding whether or not to test other animals depending on the results of these tests.

20 25 The present invention seeks to provide an apparatus in which certain components help to overcome or at least ameliorate some of the current problems associated with the monitoring of milk collected from animals such as dairy cattle.

In accordance with the present invention there is provided an animal product sampling device comprising:

30 a well arranged, in use, to collect fluid flowing through a fluid tube connected to the well;

a drain, one end of which is connected to the well, which is arranged such that, in use, fluid from the well may pass to the fluid tube connected to the well; and

35 a sample tube arranged, in use, to draw fluid from a non-turbulent zone of fluid within the well.

wherein the device is arranged such that, in use, a non-turbulent zone of fluid, from which a sample of fluid can be drawn through the sample tube, is created in the device due to the dimensions of the well and the drain.

Also in accordance with the present invention there is provided an animal product sample transportation device, the transportation device comprising:

5 a plurality of tubes of equal diameter, through each of which a sample of fluid passes in use;

control means arranged, in use, to control the flow in the tubes such that each tube can controllably retain a sample temporarily;

10 determining means arranged, in use, to determine the presence of milk in the tube at the point where it is discharged from the sample tubes;

varying means arranged, in use, to vary the speed and flow of the discharge from the sample tubes;

15 evacuating means arranged, in use, to evacuate the sample tubes to minimise the quantity of milk taken; and

washing means arranged, in use, to wash the sample tubes and remove surplus wash material.

Furthermore, in accordance with the present invention there is provided an animal product sample collecting device, the device comprising:

20 a moveable frame, supporting, in use, a plurality of removable collection vials arranged to collect, in use, animal product samples, the frame being positioned, in use, to accept, in the vials, samples from an outlet of a sample selecting device; and

a frame driver for moving the frame relative to the outlet in order to allow the samples to be dispensed into the vials.

25 The movable frame may be a rotatable carousel, and may contain removable inserts in which the vials are housed.

The invention provides a generic collection, sampling and ordering mechanism which can then be fed into a plurality of analytical devices. The sampling components and analytical devices are connected, but act independently so that sampling and analysis can be separated, if required, temporally or spatially.

30 The present invention provides a sampling regime whereby samples can be taken from selected cows and selected assays can be performed according to the requirements of the farmer and/or the economic value of the cow and/or previous analyses from the selected cow. Although the analysis of some assays must be conducted by an automated regime at fixed times, the sampling regime may also be adjustable so that the system can take and analyse a sample of milk from a selected cow when the milking machine operator demands it. By monitoring internal data which

maps the progress of a disease or the ovulation cycle, the timing of the assays may be adapted according to this previous sample data. Furthermore, by providing an adjustable sampling regime, the sensitivity of the system can be altered by the farmer or an off-site data analyst (either human or software-based) as required.

5 By providing a well, a drain and a sample tube at each sample point and by balancing the dimensions of these parts of the sample point, a non-turbulent zone of milk is created, thereby eradicating any bubbles in the sample which is drawn through the sample tubes. If these tubes are of a fixed length this ensures all of the samples taken are of an equal volume. The tubes act as temporary storage means for the 10 samples, and there is no need for a separate intermediate storage component. Furthermore, these tubes can be bundled together in order to decrease the overall size of the milking apparatus and reduce heat loss.

By controlling the exposure of certain analysers to specified samples, much of the inconvenience of conventional monitoring systems can be avoided.

15 The collector can store a number of samples in sequence and then direct them to specific analysers according to instructions from a controlling processing system. These instructions may be automated, adapted due to historical data or adapted at will by the farmer or another system operator. The collector therefore provides flexibility within the sampling regime. The provision of this component also enables the system 20 to provide multiple analyses from each milk sample or each cow as required.

Each bio-marker is tested for in a separate analyser, in which the biosensor, or alternative means for performing the assay, is housed. The analysers may use any other form of sensing technique, such as solid phase immunosensors or optical field analysis, and may or may not operate simultaneously. As will be described later, the 25 milk samples can then be diverted to specific analysers depending on which assays are required. This ensures that the samples are properly separated and are not wasted on any unnecessary assays. It is not necessary, therefore, to analyse for all conditions simultaneously. Additionally, as groups of biosensors or similar devices need not be manufactured prior to milking, the sampling regime may be adapted to include or omit 30 certain assays at will. This provides a superior and more efficient analysing regime. For example, disease assay is necessary perhaps only once a year or during the outbreak of an infectious disease, while progesterone must be routinely analysed in perhaps less than 5% of milkings, and mastitis must be tested for at frequent intervals. By providing a separate analyser for each assay, samples may be directed to these 35 easily and quickly for analysis.

The present invention will now be described with reference to the accompanying drawings, in which:

Figure 1 shows a milking apparatus according to the present invention; Figure 2 shows the workings of the apparatus of Figure 1 in greater detail; Figure 3 illustrates a sample point which is used in the apparatus of Figures 1 and 2;

5 Figure 4 illustrates a sampler which is incorporated into the apparatus of Figures 1 and 2;

Figure 5 shows the sampler and collector of Figure 2;

Figure 6 shows an identification device which is incorporated into the apparatus of Figures 1 and 2; and

10 Figure 7 shows a bleed valve which is incorporated in valves V1 to V8 of Figure 4 and Figure 5.

15 Although an apparatus in accordance with the present invention may be adapted to analyse samples from a number of different farm animals within a number of different body fluids, the invention will be described by way of illustration with respect to performing assays within the milk of dairy cows during milking within a milking parlour.

20 Figure 1 shows how the use of multiple analysers is implemented within a milking apparatus, and how certain components interact to allow for the samples to be taken, selected for analysis and directed to the correct analysers in a fixed or adaptive manner. The analysers do not necessarily operate simultaneously. Referring to Figure 1, the milking apparatus 1 is provided with sample points 3, which take samples from the milk produced by each cow 2. The samples are directed to a sampler 5 through sample tubes 4, and are then passed to a collector 7. In an alternative configuration the samples are directed to a sampler 5 through sample tubes 4, and are then either 25 returned to the main milk line through the optional milk return line 6 or selected for analysis and passed to a collector 7. The samples can then be directed to analysers 9 depending on instructions from a herd management database 8.

30 The processing system, for example a computer or a microprocessor device, has a memory unit, the memory unit storing: a database of information on individual animals; a plurality of mathematical models of bio-marker properties; and interface software, for interfacing with the sampler 5, the collector 7 and the plurality of analysers 9. Current implementations of the processing system include: embedded PCs; PC104 expansion cards; and RCom. The operating system used may be any convenient OS, for example DOS, MS Windows, UNIX/Linux, Apple, Symbian EPOC or PalmOS.

35 The processing system is programmed to receive and update information held on the animal database. Examples of the information held on the database include: age, calving information, and results of previous analysis. The processing system is

also programmed to use the mathematical models to relate the measured concentration of specified bio-markers to fertility, wellness or disease status.

Information can be passed from the herd management database 8 to the sampler 5 and collector 7. The system also provides a manual "over-ride" option, the 5 form of a button, for example, which allows the farmer to check the fertility (confirmation of insemination day) or disease status of a specific animal.

Figure 2 shows the workings of the apparatus in greater detail. Once the animal comes into the stall to be milked it is identified, a cluster is attached to the cow and milking can begin. The system is monitored so that, at a specific point after 10 attachment or once a set volume of milk has been collected, sampling can begin.

Figure 1 shows how a milk sample is drawn from the milk tube into the sampler, collector and analyser using positive pressure. Figure 1 shows how, in an alternative example of an apparatus, a small proportion of the milk from each milk line is passively diverted and flows in a parallel system to the main milk flow. This milk, by default, is 15 returned back to the system, either to each individual milk line or to a receiver vessel. The diverted milk tubes pass through a sampler 5 which is capable of taking samples from an individual milk tube when instructed. This system allows a small aliquot of milk to be taken from any animal when required with minimum milk loss.

Milk is therefore either generically sampled and returned to the milk line when 20 it is not selected to move on to the analysers (passive sampling), or alternatively only certain lines are sampled (active sampling). These options mean that milk which is not specifically used for an assay is not wasted. This is essential when analyses are frequent, as the cost of the lost milk may outweigh that of the analysis.

The sample points 3 of the apparatus may be positioned before or after, or 25 integrated into, any device in the milk line. An example of a sample point is shown in Figure 3. The sample point 3 is based on a well 13 set in the long milk tube 14 with a drain 15 which returns milk and wash water downstream. The sample is drawn through a tube suspended from the top of the well 13. The correct balance of depth of well 13 and size of drain 15 creates a non-turbulent zone of milk for drawing a sample which 30 is free of bubbles. Depending on the set-up of the sample point 3, the device can be attached at an angle of between 0° and 90° to the vertical. The sample tube could also enter from below. The internal diameter of the sample tube is preferably between 1mm and 3mm. Additionally, the device may further include a controlled valve or a non-return valve, in order to ensure efficient sampling, if required.

Once each of the required samples has been taken it is passed to the sampler 35 5 via a tube 4. In the favoured method these tubes 4 may be of any length. In the alternative method these tubes 4 may be of the same length or a known length, and

may be used for temporarily storing milk samples of a known volume before they pass to the sampler 5. In prior art systems, the tubes differ in length depending on where the sample point and sampler are located within the milking apparatus, and are used as a transportation means only, such systems therefore require additional temporary storage means. The fixed, known length tubes 4 of the apparatus 1, however, act as a temporary storage device, as tubes which are of a known length may store a known volume of sample. The tubes 4 are preferably also between 1mm and 3mm in diameter each, and may be lagged or bundled together and insulated to prevent significant heat loss.

Figure 4 shows examples of samplers. The sampler 5 receives samples from the sample points 3 and then directs these, depending on controller instructions, to the collector 7. Figures 4A and 4B show a sampler 5 to which all the milk samples flow (or are pumped) through their respective tubes 4. The samples may flow into a manifold 16 and then together into a single milk sample line 17. A rotating valve system may also be employed, so that some or all of the milk samples flow together and by default flow into a single tube which goes back to the milking system or to waste. Alternatively, as shown in Figure 4C, the tubes 4 along which the milk passes after it has been collected at the sample point 3 can each have a diverting valve which allows a small quantity of milk to be taken if required. Samples which are selected for analysis are then passed to a collector 7 via a peristaltic pump 10, as shown in Figure 2.

An example of a collector, to which the selected samples are directed, is shown in Figure 5. The device contains a number of inserts 19 which in turn each hold a collection vial 20. The collector 7 collects a number of samples in vials 20 (as instructed), and each insert 19 within the collector 7 can be removed, either individually or within a carousel, for processing, analysis or storage. The inserts are temperature controlled to ensure accuracy of measurement. The carousel 28 is driven by a motor (not shown). The collector 7 can therefore store a number of samples in sequence until the analyser 9 is ready to conduct the required assay. Each collection vial 20 is indexed, and the system is able to store a record of what sample is within each. Additionally, an array of electrodes can be mounted in the collector 7 to determine the electrochemical properties of the milk in the sample. Once the collector 7 receives instructions on how to proceed with a specific sample, a motor or solenoid operated depression valve 29 is activated to allow the sample to be passed to an analyser or to waste. The sample may be removed by gravity or by a pump 18 (see Figure 2).

The use of a collector enables the system to perform multiple analyses from each milk sample or each cow. For example, multiple samples may be taken from the same vial and routed to separate analysers via a diversion valve. Alternatively, cones

21 and/or 22 positioned under the collector may receive the samples from certain vials as desired. These cones may be for use with a specific analyser, or a single cone with separate sections could be used to sub-divide a single sample into sub-samples. The use of a cone allows multiple samples to be taken from a specific cow.

5 The combination of a single sampler and a collector for multiple sample points uses electrical apparatus which is far simpler than that of prior art. The complexity, cost, size and restraints on location of this portion of the apparatus is therefore reduced.

10 The analysers to which the selected samples are sent conduct a chemical, biochemical or physical assay to measure one or more bio-marker. For this purpose each analyser can include a reaction chamber, where the assay may be carried out. The data output from the assay is communicated to the herd management processing system.

15 The analysers transmit information to the processing system to enable rapid and timely analysis of samples. This information will include the time before readiness to analyse, the type of analysis that it will conduct, the volume of sample it requires, the timing of sampling during milking, the type and number of the remaining sensors, the need for servicing and other information for it to operate.

20 Depending upon the particular assay to be performed, a biosensitive region (or biosensor) within the analyser may include one or more key elements required to measure a bio-marker, for instance assay solutions, electrodes (often made of carbon), or fixed antibodies.

25 Examples of appropriate testing techniques include chemical, biochemical and immuno-assay. As an alternative reagents may also be incorporated into the analyser itself. The reagents and the biosensors used typically have an operative range of temperatures. The analyser may further be provided with a temperature control mechanism (not shown) for maintaining its temperature at a specified level or within a predetermined range.

30 Details of measurements corresponding to each given animal are transmitted to an animal database. In a fully automated system, the test measurements are transmitted electronically as data signals for storage in a computer database.

35 The incorporation of antibodies (either deposited on the bio-sensitive region or in free solution) allows a specific immunoassay to take place within the reaction chamber and for a specific bio-marker to be measured. In certain cases, the bio-sensor measurement device includes a control reaction chamber in which measurements from a bio-sensor (in the absence of one component of the assay) will be used to remove a substantial proportion of any background signal from the milk.

Some assays do not require a bio-sensor (or use a bio-sensor but require no antibodies) and will measure a bio-marker directly in the milk utilising a chemical or physical reaction. Examples of such assays include: an enzymatic reaction catalysed by an enzyme in the milk; or a specific wavelength of the electromagnetic spectrum correlating to the concentration of a known bio-marker.

Preferably, the automated sample processing arrangement includes a cow identification device, which identifies which cow is being milked and in which stall the cow is being milked. Identification data may be gathered automatically. An example of such a device and how it can be applied to the milking apparatus are shown in Figures 6 and 2, respectively. Each animal is fitted with a transponder 23 (see Figure 1) whose signal is received by an antenna 24 in its respective stall, and this antenna 24 is coupled to the identification device via cables. A multiplexer gathers the signals so that they can be transferred to the processing system simultaneously. Alternatively the data may be gathered manually, for instance through data entry into a mobile terminal device with a communication link to the herd management processing device or through a conventional computer keyboard plugged into the herd management processing system. The identification device will therefore communicate directly or indirectly with the herd management system.

The cow identification device gathers cow identification information (whether manually or automatically) thereby recognising which cow is being milked and in which milking stall.

Cow identification information is transferred to the herd management processing system, which accesses the cow database to retrieve data relating to the identified cow and the mathematical models for specified bio-marker properties. The processing system then analyses: information on the cow; parameters set by the farmer; the models of specified bio-markers; measurement regimes and other information. Next the processing system determines whether a sample of milk from that cow should be used for measuring one or more bio-marker.

The sample point takes a sample of milk from the milk line while the, now identified, cow is being milked. This sampling may occur for all cows or for only specified cows. As described above, the sample from all of the sample points is directed to the sampler.

Figure 7 shows a continuous flow (or bleed) valve 30 that is inserted in the normally open path of valves V1 to V8, that are a part of the sampler 5. When no sample is being taken this device clears the sample tube of any residual milk by drawing air. The diameter of the holes are optimised to ensure that air ingress from

the multiplicity of sampling points does not reduce the vacuum reserve below that specified in ISO 5707.

Depending upon the instructions received from the herd management processing system, the sampler 5 directs the samples to either the milk line, waste or 5 a specific analyser.

When samples are directed to the analyser, it conducts a chemical, biochemical or physical assay and measures a specific bio-marker in that milk sample. The herd management processing system determines which assay or assays are to be conducted and hence which analyser the sample is directed to. The data output of the 10 assay will be communicated to the herd management processing system.

The herd management processing system will then process the results of the assay, using the embedded mathematical models of specified bio-markers and stored animal data relating to that specific cow. The processing system is preferably programmed to present a graphical user interface to allow the farmer to access the 15 acquired information and ultimately to assess the status of his herd. If any urgent actions are required, the processing system is advantageously programmed to alert the operator and to suggest what action may be required, for example; "cow A3 (currently in stall 5) is ovulating, contact the AI (artificial insemination) professional within 24 hours", or "cow F5 is not ovulating as normal, contact the veterinarian". In this case, 20 the milk of other cows which may be affected (for example in the case of a disease), can be sampled and analysed quickly, accurately and on demand.

The processing system may furthermore be in communication with wireless and/or wire networks of computing devices. The processing system can then generate and send text messages directly to a wireless communicator device (for instance, a 25 mobile telephone or a personal communication device) to report the status of an individual cow or of the whole herd. Likewise processing system can send a request for action directly to a third party (for example an email message to a veterinarian or an AI professional).

As might be expected, the processing system is preferably programmed to be 30 able to change the sensitivity and frequency of measurements of any given bio-marker. The software running on the processing system is preferably capable of learning and adapting to the requirements of each individual cow.

By providing an integrated, hygienic wash system, which is co-ordinated with conventional milking machine wash cycles, the sample points 3, tubes 4, the sampler 35 5, the collector 7 the analysers 9 can be washed out between milk sampling and/or at the completion of the milking of the herd.

The tubes 4 between the sample point 3 and the sampler 5 are washed by sensing when the milk machine is being washed, either through integration with the milk machine control system or by employing a vacuum sensor or other sensor. A small amount of washing fluid from the milk line is then drawn through the tubes 4 and sampler 5 automatically during the circulation cleaning of the entire milking apparatus.

5 Alternatively, a wash line is inserted at each sample point 3.

A three-way valve and wash line is inserted between the sampler 5 and collector 7 of the second milking apparatus, in order to wash these components. This provides an option as to which of the two components is washed. By providing a wash

10 tube 25 above one of the collection vials 20 which is capable of spraying wash fluid at an angle, a "swirling" effect is produced which effectively cleans the vial 20 and the cones 22. Washing fluid can enter and exit the sampler 5 or collector 7 via an internal wash line 26. The pump 10, its inlet and outlet and cone 21 are cleaned between samples by opening valves V9 and V10 when no vial is present in the position above

15 cone 21. In the case of the collector 7, a valve 27 can control access of the washing fluid to the vials in order to protect against contamination of the milk from the washing fluid. Furthermore, each analyser 9 has its own wash system. By giving each component of the apparatus 1 its own wash system in this way, the parts of the device may be washed individually as needed or desired.

20 Each analyser's wash system, which is separate to that of the collector 7, as the analyser runs in parallel to the milking process and may not therefore be ready for cleaning at the same time as the rest of the apparatus: milking may finish before or after the analysis cycle.

Once washing of a component or set of components has been completed, the

25 used washing fluid is discharged to waste. If every cow is to be sampled passively, for example in the case of testing for mastitis, then the whole sample tube will not have to be filled with milk and the last sample will have to be drawn through using water from the wash cycle. This will reduce the cost per sample. In the favoured active method milk loss is minimised

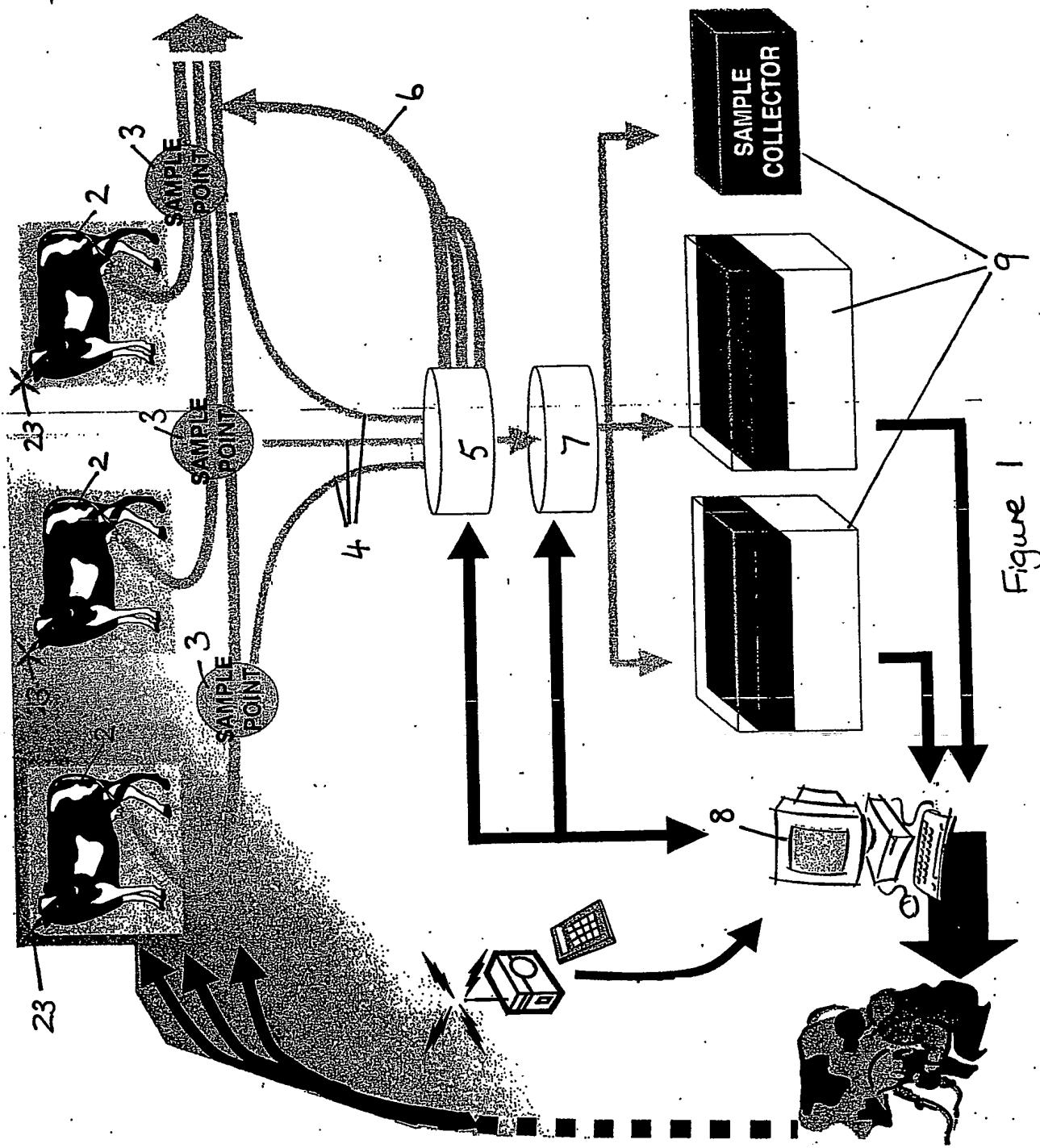
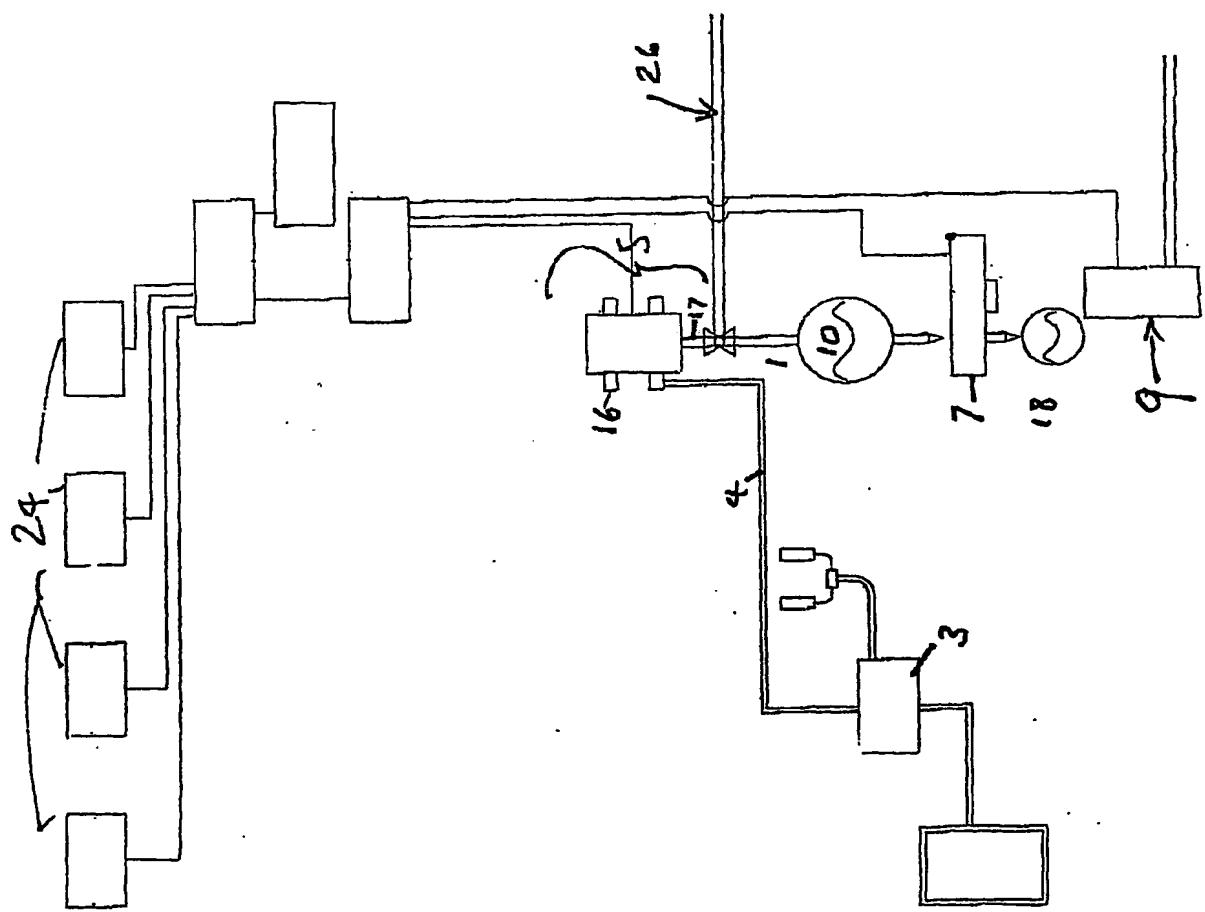


Figure 2



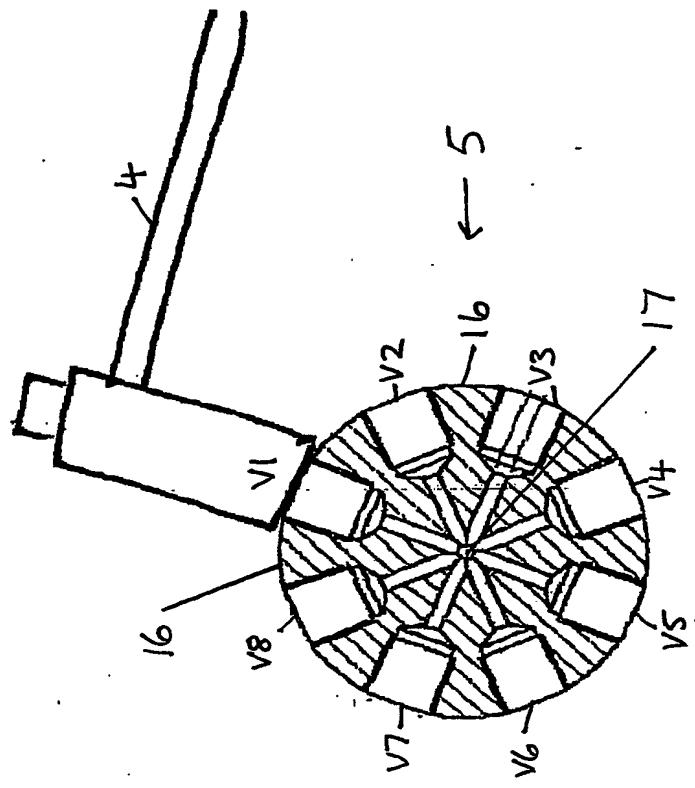


Figure 4A

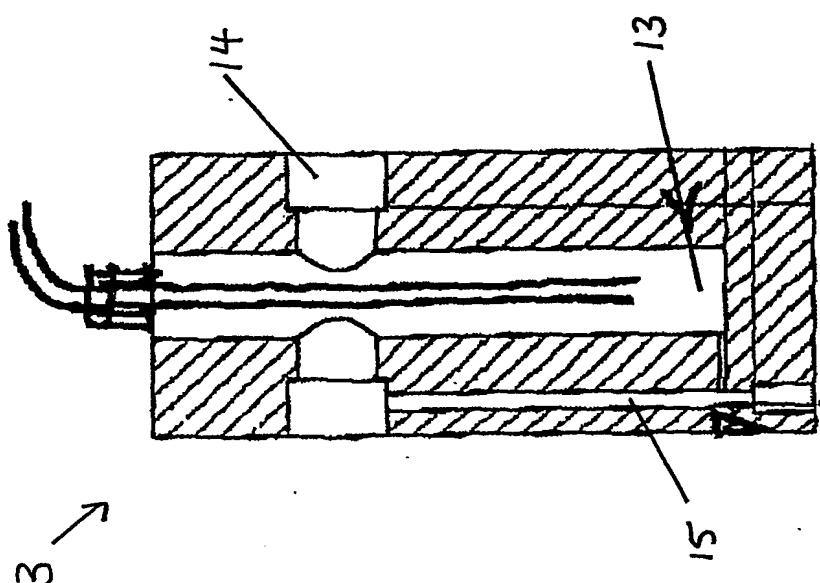


Figure 3

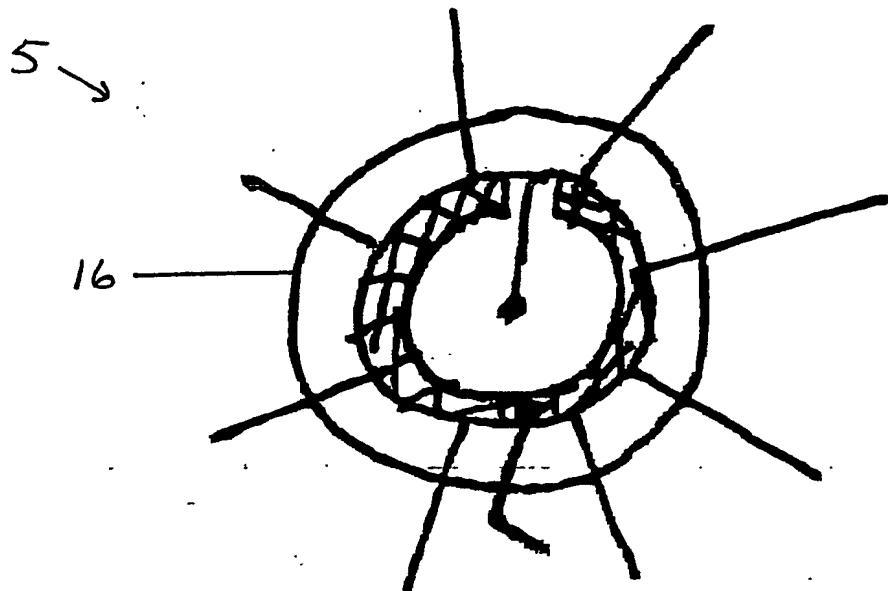


Figure 4B

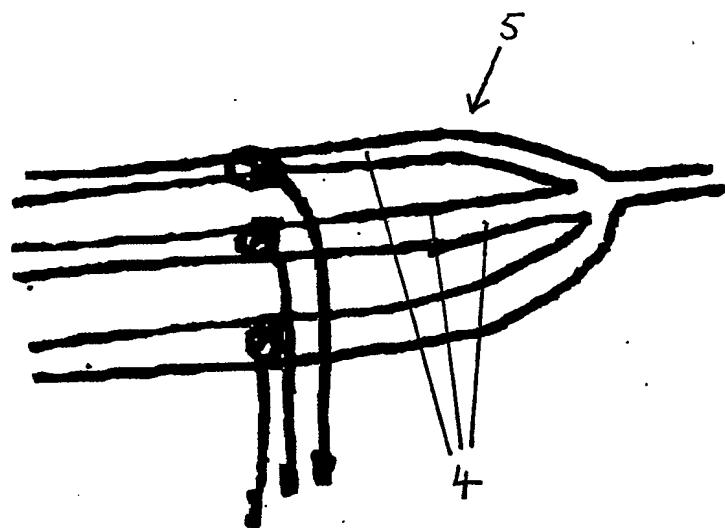


Figure 4C

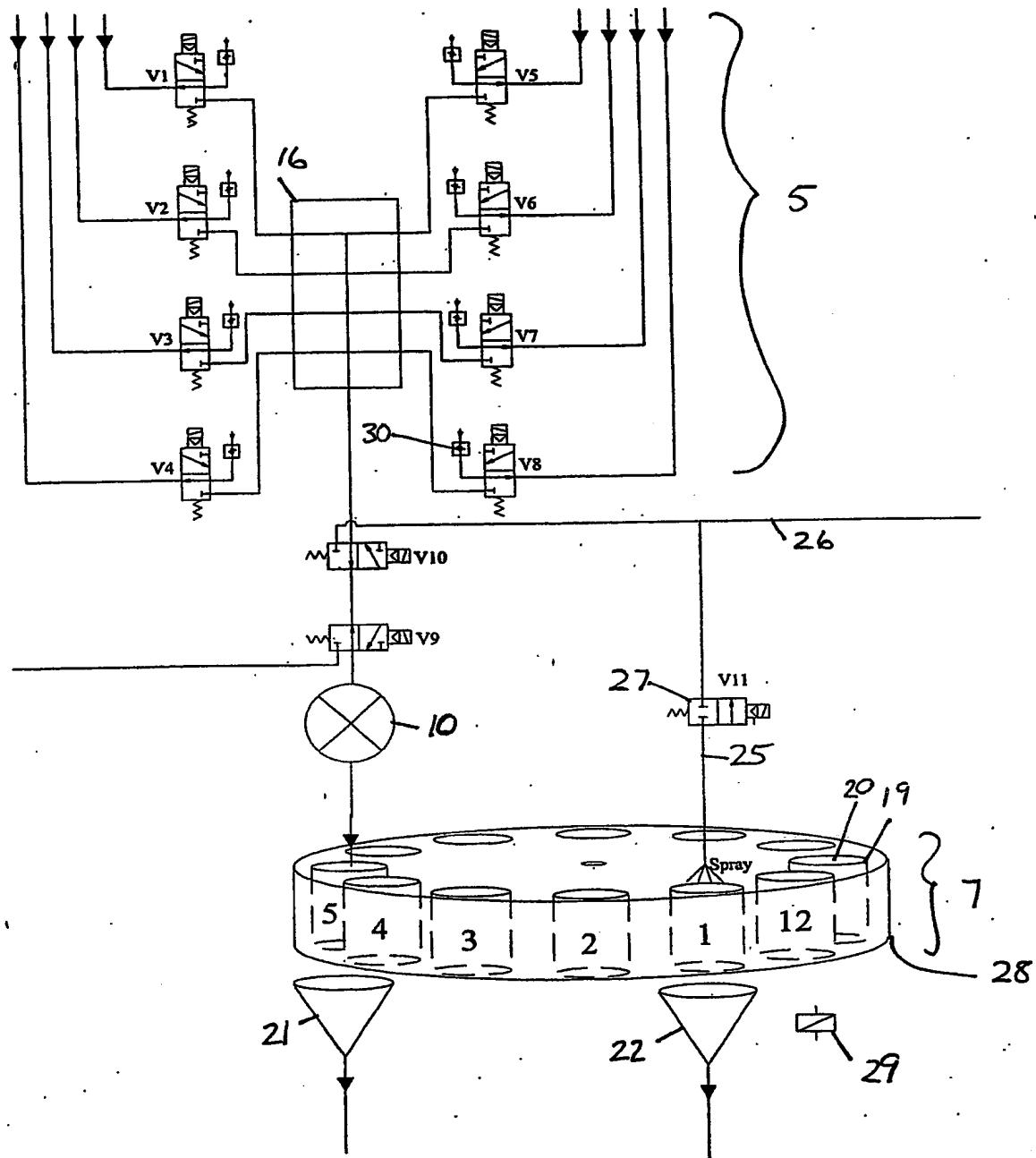


Figure 5

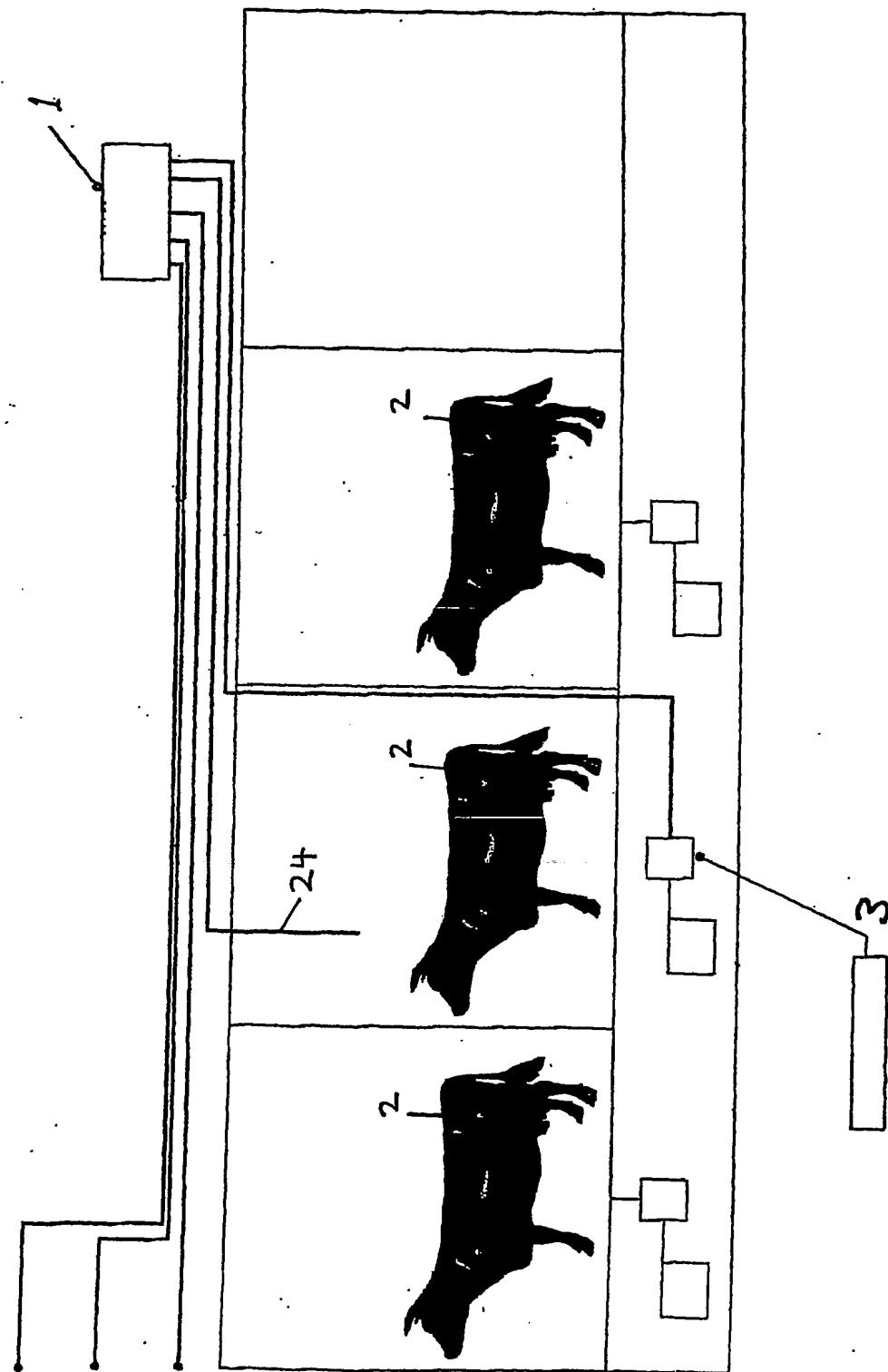


Figure 6

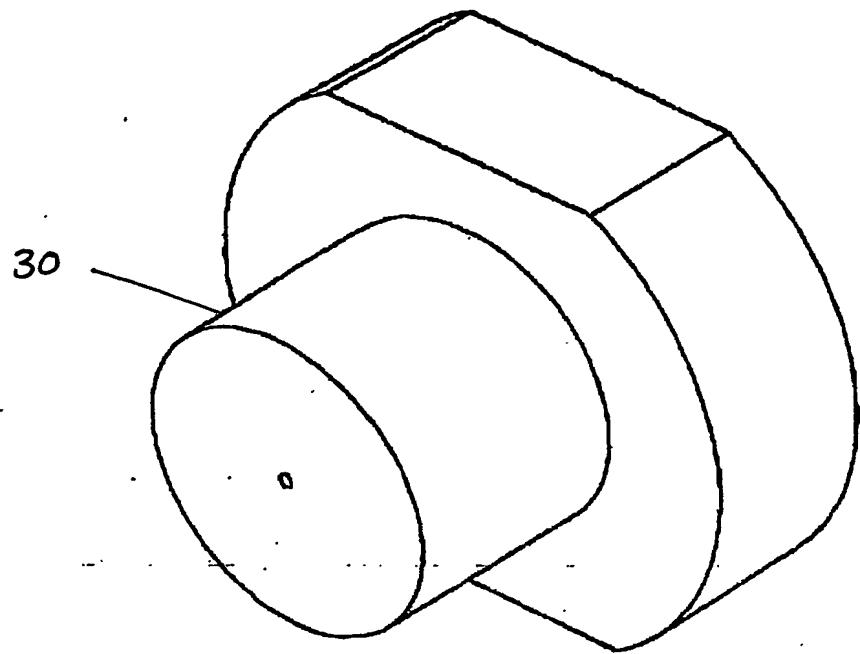
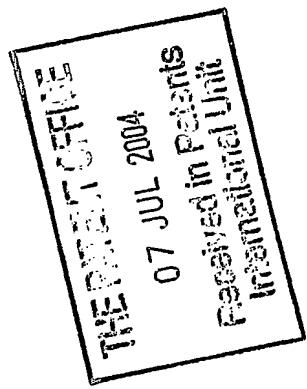


Figure 7

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